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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,973	06/26/2006	Barbara Ensoli	50318/013001	3019

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EXAMINER	
KASSA, TIGABU	

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
06/26/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/577,973	ENSOLI ET AL.	
	Examiner	Art Unit	
	TIGABU KASSA	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *9 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/22/08 and 12/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23 are pending. Claims **1-8 and 10-15** are under consideration in the instant office action. Claims 9 and 16-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claims. Claims 21-23 are cancelled.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-8 and 10-15) in the reply filed on 04/13/09 is acknowledged.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

The information disclosure statement (IDSs) submitted on 01/22/08 and 12/19/07 is noted and the submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the references.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Laus et al. (Journal of Controlled Release 2001, 72, 225-309) as evidenced by Specification and test methods for EUDRAGIT® L 100-55, Degussa.

Applicants claim nanoparticles comprising a core of a water insoluble polymer or copolymer and a shell of a hydrophilic polymer or copolymer comprised of the specified monomers. Further limitations specify the monomers used to form the core polymers.

Laus et al. disclose microspheres with a hydrophilic and protein-friendly surfaces as protein delivery systems prepared by dispersion polymerization (page 280, title). The cores are made of either polystyrene or methylmethacrylate (page 280, introduction). The methylmethacrylate microspheres are coated with a steric stabilizer of Eudragit L100/55. The Eudragit polymer is a methlacrylic acid ethylmethacrylate as evidenced by Specification and Test methods for Eudragit L100-55 (section 2, Chemical structure), Degussa.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness

Claim 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laus et al. (Journal of Controlled Release 2001, 72, 225-309).

Applicant Claims

The limitations of instant claim 1 are set forth above. Instant claim 7 recites the nanoparticles of claim 1 wherein the particle diameter is 50-1000 nm.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Laus et al. are set forth above. Laus et al. also teaches a particle size distribution of 0.5 to 20 microns in diameter (page 280, introduction).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Although Laus et al. teach the particle size in overlapping ranges, Laus et al. do not teach the size in anticipating range.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to one of ordinary in the art at the time the invention was made to produce the invention in the particle size as recited, because Laus et al. teach similar composition in overlapping particle size range. The skilled artisan would have been motivated to select a particle size range which is suitable for administration to animals or humans since the work of Laus et al. is presented in an article entitled Novel Therapeutic Delivery Systems which is found in the Journal of Controlled Release. The skilled artisan would have a reasonable expectation of success at optimizing the particle sizes of the nanoparticles since such routine optimization is within the purview of the skilled artisan.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Claim 4 is rejected 35 U.S.C. 103(a) as being unpatentable over Laus et al. (Journal of Controlled Release 2001, 72, 225-309) as applied to claims 1-3 and 5 above, and further in view of Schacht et al. (US Patent 6312727).

Applicant Claims

The limitations of instant claim 1 are set forth above. Instant claims 4 and 6 further specify the monomers used to form the nanoparticles.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Laus et al. are set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Laus et al. do not teach the specific monomers recited in the instant claims. This deficiency is cured by Schacht et al.

Schacht et al. teach polymer-based carrier vehicles for the delivery of nucleic acid material to target cells (abstract). The outer protective shield of the delivery system may be based on acrylic or methacrylic monomers have reactive amino or alkyl amino functional groups (abstract and column 19, lines 19-21). Specifically such monomers may include acrylic or methacrylic monomers terminating in an alkyl amino group (column 19, lines 35-41).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to one of ordinary in the art at the time the invention was made to select a monomer which is a derivative of a methacrylic acid since Laus et al. already teach the use of methacrylic acid monomers for coating the nanoparticles. The skilled artisan would have been motivated to use polymers with reactive alkyl amino functional groups (which would include those monomers found in instant claims 4 and 6) since they are taught by Schacht et al. as being suitable for bonding and forming a protective coating or shield (abstract and column 19, lines 22-25). The skilled artisan would have a reasonable expectation of success at combining the prior art teachings since the Laus et al. and Schacht et al. both use similar polymers for coating vehicles or particles for use with biological macromolecules.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim 6 is rejected 35 U.S.C. 103(a) as being unpatentable over Laus et al. (Journal of Controlled Release 2001, 72, 225-309) as applied to claims 1-3 and 5 above, and further in view of Jon et al. (Langmuir, 19, 9989-9993, 2003).

Applicant Claims

The limitations of instant claim 1 are set forth above. Instant claim 6 further specifies the monomers used to form the nanoparticles.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Laus et al. are set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Laus et al. do not teach the specific monomers recited in the instant claims. This deficiency is cured by Schacht et al.

Jon et al. teach nonbiofouling polymeric self-assembled monolayers (title). One of the antifouling polymers comprises polyethylene glycol methyl ether methacrylate (page 9990). The polymer coating reduces the absorption of nonspecific polymer (figure 2, page 9992).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to one of ordinary in the art at the time the invention was made to incorporate polyethylene glycol methyl ether methacrylate for use as a coating since it is taught as a suitable polymer for creating nonfouling surfaces by Jon et al. The skilled artisan would have been motivated to incorporate polyethylene glycol methyl ether methacrylate monomers to control the amount of protein immobilized on the microspheres. Additionally, the antifouling properties of the polyethylene glycol would prevent the adsorption of unwanted biopolymers upon administration of the microsphere to a subject. The skilled artisan would have a reasonable expectation of success at incorporating the polyethylene glycol methyl ether methacrylate since Laus et al. already teaches the use of copolymers comprising methacrylate.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Claim 8 is rejected 35 U.S.C. 103(a) as being unpatentable over Laus et al. (Journal of Controlled Release 2001, 72, 225-309) as applied to claims 1-3 and 5 above, and further in view of Melker et al. (US Patent No. 6974706) .

Applicant Claims

The limitations of instant claim 1 are set forth above. Instant claim 8 further specifies the nanoparticles further comprise a fluorescent chromophore.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Laus et al. are set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Laus et al. do not teach the incorporation of a fluorescent chromophore. This deficiency is cured by Melker et al.

Melker et al. teach nanotechnology, in particular nanoparticles, offers many advantages when used for applications such as the delivery of bioactive agents (i.e., DNA, AIDS drugs, gene therapy, immunosuppressants, chemotherapeutics), and drug uptake and degradation (i.e., enzyme encapsulation). For example, nanoparticles have been proposed as providing site-specific distribution of drugs to, and minimization of loss from, a target site. Appropriately sized particles have been proposed wherein such particles can be delivered to selected tissues to release their drug load in a controlled and sustained manner (column 1, lines 32-42). Melker et al. teach a unique method for diagnosing a condition and/or disease in a patient by utilizing a nanoparticle-based biosensor that includes nanoparticles, aptamers, and volatile or "surrogate" biomarkers. Melker et al. teach the incorporation of the so called molecular beacons such as chromophores to provide a means for signaling and quantifying detected target analytes/biomarkers in exhaled breath (column 6, lines 35-38).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to one of ordinary in the art at the time the invention was made to incorporate fluorescent chromophore in nanoparticulate based systems because Melker et al. teach the incorporation of chromophores in nanoparticles. The skilled artisan would have been motivated to incorporate fluorescent chromophore to

provide a means for signaling and quantifying detected target analytes/biomarkers (column 6, lines 35-38). The skilled artisan would have a reasonable expectation of success at incorporating fluorescent chromophore since Melker et al. already teaches the use of chromophores for detection in similar nanoparticulate systems.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 10-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laus et al. as applied to claims 1-3 and 5 above, and further in view of Le Buanec et al. (Biomedicine and Pharmacology 2001, 55, 316-320).

Applicant Claims

The limitations of instant claim 1 are set forth above. Instant claim 10 recites the nanoparticle of claim 1 which further comprises a pharmacologically active agent absorbed on the surface. Instant claim 11 further specifies the agent is a disease associated antigen while claims 12 and 14-15 further specify the type of antigen.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Laus et al. are set forth above.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Laus et al. do not specifically teach the absorption of a pharmaceutically active agent such as an antigen. This deficiency is cured by Le Buanec et al.

Le Buanec et al. teach the use of microspheres for the administration of Tat toxoid (Materials and methods; Immunogen preparation).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to one of ordinary skill in the art at the time of the present invention was made to incorporate HIV Tat toxin in the since Le Buanec et al. teach the use of microparticles for the administration of HIV Tat toxin. The skilled artisan would have been motivated to use the microparticles of Laus et al. for the formation of a vaccine using Tat toxin since Le Buanec et al. teach that Tat toxin is advantageously administered in such a way as to produce a mucosal immune response. The skilled artisan would have had a reasonable expectation of success in incorporating HIV Tat toxin since Laus et al. already teaches that the microparticles are suitable for protein absorption.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Claims 1-8 and 10-15 are rejected. Claims 9 and 16-20 are withdrawn. Claims 21-23 are cancelled. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIGABU KASSA whose telephone number is (571)270-5867. The examiner can normally be reached on 9 am-5 pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tigabu Kassa 06/20/09

/Mina Haghighatian/
Primary Examiner, Art Unit 1616